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TITLE: Methods for inducing a mucosal immune response

DATE-ISSUED: October 3, 2000

INT-CL: [7] A61K 39/00
US-CL-ISSUED: 424/184.1; 424/199.1, 424/234.1, 424/278.1, 424/282.1, 424/812, 514/44
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DIALOG(R)File 155:MEDLINE(R)

10476798 20341707

Helicobacter **pylori-induced mucosal inflammation is** Th1 **mediated and exacerbated in IL-4, but not IFN-gamma, gene-deficient mice.**

Smythies LE; Waites KB; Lindsey JR; Harris PR; Ghiara P; Smith PD
Department of Medicine, Pathology, and Comparative Medicine, University of Alabama, Birmingham, AL 35294, USA.

Journal of immunology (UNITED STATES) Jul 15 2000, 165 (2) p1022-9, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: DE-72621, DE, NIDR; DK-54495, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 0010
Subfile: INDEX MEDICUS; AIM

To elucidate the pathogenesis of **Helicobacter** pylori-associated gastritis, we studied immune responses of C57BL/6J wild-type (WT), SCID, and gene deficient (IFN-gamma-/- and IL-4-/-) mice following infection with a pathogenic isolate of H. pylori (SPM326). During early infection in WT mice, mononuclear and polymorphonuclear cells accumulated in the gastric lamina propria, and the numbers of cells in the inflamed mucosa expressing IFN-gamma, but not IL-4, mRNA rose significantly ($p < 0.005$), consistent with a local Th1 response. Splenic T cells from the same infected WT mice produced high levels of IFN-gamma, no detectable IL-4, and low amounts of IL-10 following in vitro H. pylori urease stimulation, reflecting a systemic Th1 response. Infected C57BL/6J SCID mice did not develop gastric inflammation despite colonization by many bacteria. Infected C57BL/10J and BALB/c mice also did not develop gastric inflammation and displayed a mixed Th1/Th2 splenic cytokine profile. These data imply a major role for the Th1 cytokine IFN-gamma in H. pylori-associated gastric inflammation in C57BL/6J mice. Compared with WT animals, infected IL-4-/- animals had more severe gastritis and higher levels of IFN-gamma production by urease-stimulated splenocytes ($p < 0.01$), whereas IFN-gamma-/- mice exhibited no gastric inflammation and higher levels of IL-4 production by stimulated splenocytes. These findings establish C57BL/6J mice as an important model for H. pylori infection and demonstrate that up-regulated production of IFN-gamma, in the absence of the opposing effects of IL-4 (and possibly IL-10), plays a pivotal role in promoting H. pylori-induced mucosal inflammation.

Descriptors: Gastric Mucosa--Pathology--PA; *Gastritis--Immunology--IM; ***Helicobacter** pylori--Immunology--IM; *Interferon Type II--Deficiency--DF; *Interferon Type II--Genetics--GE; *Interleukin-4--Deficiency--DF; *Interleukin-4--Genetics--GE; *Th1 Cells--Immunology--IM; Animal; Cells, Cultured; Gastric Mucosa--Immunology--IM; Gastric Mucosa--Metabolism--ME; Gastric Mucosa--Microbiology--MI; Gastritis--Genetics--GE; Gastritis --Microbiology--MI; Gastritis--Pathology--PA; **Helicobacter** pylori --Growth and Development--GD; **Helicobacter** pylori--Pathogenicity--PY; Interferon Type II--Biosynthesis--BI; Interleukin-10 --Antagonists and Inhibitors--AI; Interleukin-10--Biosynthesis--BI; Interleukin-4--Antagonis ts and Inhibitors--AI; Interleukin-4--Biosynthesis--BI; Lymphocyte Count; Male; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Mice, Knockout; Mice,

SGID; RNA, Messenger--Biosynthesis--BI; Spleen--Cytology--CY; Spleen --Immunology--IM; Spleen--Metabolism--ME; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.; T-Lymphocytes --Immunology--IM; T-Lymphocytes--Metabolism--ME
CAS Registry No.: 0 (Interleukin-4); 0 (RNA, Messenger); 130068-27-8 (Interleukin-10); 82115-62-6 (Interferon Type II)

1/9/2
DIALOG(R)File 155:MEDLINE(R)

10283895 20115505
A predominant Th1 type of immune response is induced early during acute Helicobacter **pylori infection in rhesus macaques.**
Mattapallil JJ; Dandekar S; Canfield DR; Solnick JV
Department of Internal Medicine, Division of Infectious Diseases, University of California Davis, Davis, California 95616, USA.
Gastroenterology (UNITED STATES) Feb 2000, 118 (2) p307-15, ISSN 0016-5085 Journal Code: FH3
Contract/Grant No.: RO1 AI42081, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 0004
Subfile: AIM; INDEX MEDICUS
BACKGROUND & AIMS: The immune response of gastric T cells during acute **Helicobacter** pylori infection has not been previously characterized. The aim of this study was to delineate the phenotypic and functional responses of gastric T cells during acute H. pylori infection of rhesus macaques. METHODS: Four monkeys were experimentally infected with H. pylori. Gastric biopsy specimens and peripheral blood samples were obtained 1 and 12 weeks after inoculation. Samples from 3 animals uninfected with H. pylori served as controls. The immunophenotypic changes and functional potential of CD4(+) and CD8(+) T cells in gastric mucosa and peripheral blood to produce cytokines (interleukin [IL]-2, IL-4, IL-13, interferon [IFN]-gamma, MIP-1beta, and tumor necrosis factor [TNF]-alpha) were determined at a single cell level using flow cytometry. RESULTS: An increase in CD4(+) T cells occurred in the gastric mucosa during acute H. pylori infection as early as 1 week after infection. Acute infection was characterized by a predominantly T helper (Th)1 (IL-2 and IFN-gamma) and proinflammatory (TNF-alpha and MIP-1beta) type of cytokine response and the absence of a Th2 type of response. CONCLUSIONS: A predominant Th1 type response was induced early during acute H. pylori infection and may contribute to the development of gastric disease.
Tags: Animal; Support, U.S. Gov't, P.H.S.
Descriptors: Cytokines--Biosynthesis--BI; *Gastric Mucosa--Immunology--IM ; * **Helicobacter** pylori; * **Helicobacter** Infections--Immunology--IM; *T-Lymphocytes--Immunology--IM; *Th1 Cells--Immunology--IM; Acute Disease; Biopsy; CD4-Positive T-Lymphocytes--Immunology--IM; CD8-Positive T-Lymphocytes--Immunology--IM; Flow Cytometry; Gastric Mucosa--Pathology --PA; **Helicobacter** Infections--Blood--BL; **Helicobacter** Infections --Pathology--PA; Immunophenotyping; Interferon Type II--Biosynthesis--BI; Interleukins--Biosynthesis--BI; Macaca mulatta; Macrophage Inflammatory Protein-1--Biosynthesis--BI; Th2 Cells--Immunology--IM; Tumor Necrosis Factor--Biosynthesis--BI
CAS Registry No.: 0 (Cytokines); 0 (Interleukins); 0 (Macrophage Inflammatory Protein-1); 0 (Tumor Necrosis Factor); 82115-62-6 (Interferon Type II)

1/9/3
DIALOG(R)File 155:MEDLINE(R)

10191566 20046085
Th1/**Th2 cells.**

.Romagnani S
Department of Internal Medicine, University of Florence, Italy.
Inflammatory bowel diseases (UNITED STATES) Nov 1999, 5 (4) p285-94, ISSN 1078-0998 Journal Code: C2I
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
JOURNAL ANNOUNCEMENT: 0002
Subfile: INDEX MEDICUS

A large body of evidence indicates the existence of functionally polarized CD4+ T-cell responses based on their profile of cytokine secretion. Type 1 T helper (Th1) cells produce interferon-gamma, interleukin (IL)-2, and tumour necrosis factor (TNF)-beta, which activate macrophages and are responsible for cell-mediated immunity and phagocyte-dependent protective responses. By contrast, type 2 Th (Th2) cells produce IL-4, IL-5, IL-10, and IL-13, which are responsible for strong antibody production, eosinophil activation, and inhibition of several macrophage functions, thus providing phagocyte-independent protective responses. Th1 cells mainly develop following infections by intracellular bacteria and some viruses, whereas Th2 cells predominate in response to infestations by gastrointestinal nematodes. Polarized Th1 and Th2 cells not only exhibit different functional properties, but also show the preferential expression of some activation markers and distinct transcription factors. Several mechanisms may influence the Th cell differentiation, which include the cytokine profile of "natural immunity" evoked by different offending agents, the nature of the peptide ligand, as well as the activity of some costimulatory molecules and microenvironmentally secreted hormones, in the context of the individual genetic background. In addition to playing different roles in protection, polarized Th1-type and Th2-type responses are also responsible for different types of immunopathological reactions. Th1 cells are involved in the pathogenesis of organ-specific autoimmune disorders, Crohn's disease, **Helicobacter** pylori-induced peptic ulcer, acute kidney allograft rejection, and unexplained recurrent abortions. In contrast, allergen-specific Th2 responses are responsible for atopic disorders in genetically susceptible individuals. Moreover, Th2 responses against still unknown antigens predominate in Omenn's syndrome, idiopathic pulmonary fibrosis, and progressive systemic sclerosis. Finally, the prevalence of Th2 responses may play some role in a more rapid evolution of human immunodeficiency virus infection to the full-blown disease. The Th1/Th2 paradigm also provides the rationale for the development of new types of vaccines against infectious agents and of novel strategies for the therapy of allergic and autoimmune disorders. (131 Refs.)

Tags: Animal; Human
Descriptors: *Th1 Cells--Immunology--IM; *Th2 Cells--Immunology--IM; Acquired Immunodeficiency Syndrome--Immunology--IM; Autoimmune Diseases --Immunology--IM; Chronic Disease; Hypersensitivity--Immunology--IM; Inflammatory Bowel Diseases--Immunology--IM; Sensitivity and Specificity; Th1 Cells--Physiology--PH; Th2 Cells--Physiology--PH

1/9/4
DIALOG(R)File 155:MEDLINE(R)

10017031 99319791
Poliovirus replicons encoding the B subunit of Helicobacter **pylori urease elicit a** Th1 **associated immune response.**
Novak MJ; Smythies LE; McPherson SA; Smith PD; Morrow CD
Department of Microbiology, University of Alabama at Birmingham 35294, USA.
Vaccine (ENGLAND) May 14 1999, 17 (19) p2384-91, ISSN 0264-410X Journal Code: X6O
Contract/Grant No.: AI-25005, AI, NIAID; AI-28147, AI, NIAID; DK-54495, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE

.JOURNAL ANNOUNCEMENT: 9911
Subfile: INDEX MEDICUS

The development of a vaccine for **Helicobacter** pylori is a key strategy for reducing the worldwide prevalence of H. pylori infection. Although immunization with recombinant B subunit of H. pylori urease (ureB) has yielded promising results, for the most part, these studies relied on the use of strong adjuvant, cholera toxin, precluding the use in humans. Thus, the development of new vaccine strategies for H. pylori is essential. Previous studies from our laboratory have described a vaccine vector based on poliovirus in which foreign genes are substituted for the poliovirus capsid genes. The genomes encoding foreign proteins (replicons) are encapsidated into authentic poliovirions by providing the capsids in trans. To test the utility of replicons as a vaccine vector for H. pylori, a replicon was constructed which encodes ureB. Expression of ureB in cells from the replicon was demonstrated by metabolic labeling followed by immunoprecipitation with anti-urease antibodies. To investigate the immunogenicity of the replicons, mice containing the transgene for the receptor for poliovirus were immunized via the intramuscular route. Mice given three doses of replicons did not develop substantial antibodies to ureB as determined by Western blot analysis using lysates from H. pylori. In contrast, mice given two doses of replicon followed by a single injection of recombinant ureB developed serum antibodies to ureB which were predominately IgG2a. Splenic lymphocytes from mice immunized with replicons alone, or replicons plus recombinant ureB produced abundant interferon-gamma and no detectable interleukin-4 upon stimulation with recombinant ureB. These results establish that poliovirus replicons encoding H. pylori ureB are immunogenic and induce primarily a T helper 1 associated immune response.

Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: **Helicobacter** pylori--Genetics--GE; *__Helicobacter__ pylori --Immunology--IM; * **Helicobacter** Infections--Immunology--IM; * **Helicobacter** Infections--Prevention and Control--PC; *Polioviruses --Genetics--GE; *Replicon--Immunology--IM; *Th1 Cells--Immunology--IM; *Urease--Genetics--GE; *Urease--Immunology--IM; Antibodies, Bacterial --Biosynthesis--BI; Bacterial Proteins--Biosynthesis--BI; Bacterial Proteins--Genetics--GE; Bacterial Proteins--Therapeutic Use--TU; Bacterial Vaccines--Genetics--GE; Bacterial Vaccines--Immunology--IM; Blotting, Western; Capsid--Biosynthesis--BI; Capsid--Genetics--GE; Capsid --Immunology--IM; DNA, Bacterial--Genetics--GE; DNA, Bacterial --Therapeutic Use--TU; DNA, Viral--Immunology--IM; Interferon Type II --Metabolism--ME; Interleukin-4--Metabolism--ME; Mice; Mice, Transgenic; Peptide Synthesis; Peptides--Genetics--GE; Peptides--Immunology--IM; Polioviruses--Immunology--IM; Precipitin Tests; Recombinant Fusion Proteins --Biosynthesis--BI; Recombinant Fusion Proteins--Blood--BL; Recombinant Fusion Proteins--Genetics--GE; Recombinant Fusion Proteins--Immunology--IM ; Vaccination--Methods--MT

CAS Registry No.: 0 (viral outer coat protein VP4); 0 (Antibodies, Bacterial); 0 (Bacterial Proteins); 0 (Bacterial Vaccines); 0 (Capsid) ; 0 (DNA, Bacterial); 0 (DNA, Viral); 0 (Interleukin-4); 0 (Peptides); 0 (Recombinant Fusion Proteins); 82115-62-6 (Interferon Type II)

Enzyme No.: EC 3.5.1.5 (Urease)

1/9/5

DIALOG(R)File 155:MEDLINE(R)

09678399 99003176

Antrum- and corpus mucosa-infiltrating CD4(+) lymphocytes in Helicobacter **pylori gastritis display a** Th1 **phenotype.**

Sommer F; Faller G; Konturek P; Kirchner T; Hahn EG; Zeus J; Rollinghoff M; Lohoff M

Institut fur Klinische Mikrobiologie, Immunologie und Hygiene der Universitat Erlangen-Nurnberg, Erlangen, Germany. sommer@mikrobio.med.uni.e

rlangen.de
Infection and immunity (UNITED STATES) Nov 1998, 66 (11) p5543-6, ISSN 0019-9567 Journal Code: GO7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9901
Subfile: INDEX MEDICUS
In this study, cytokine patterns produced by CD4(+) T cells isolated from antrum or corpus gastral biopsy specimens of 10 patients with **Helicobacter** pylori-positive gastritis were compared. To this end, expression of intracellular cytokines (interleukin-4 [IL-4] and gamma interferon) and of CD4 was assessed by flow cytometry. Ten to 60% of the isolated CD4(+) T cells produced gamma interferon upon stimulation. With the exception of one patient, IL-4-positive CD4(+) cells were not detected. Therefore, CD4(+) cells infiltrating antrum and corpus stomach mucosa during H. pylori infection show a Th1 phenotype. This polarized Th1-type response may contribute to the inability of the immune system to eradicate H. pylori infection.
Tags: Female; Human; Male; Support, Non-U.S. Gov't
Descriptors: CD4-Positive T-Lymphocytes--Immunology--IM; *Gastric Mucosa --Immunology--IM; *Gastritis--Immunology--IM; * **Helicobacter** pylori --Immunology--IM; ***Helicobacter** Infections--Immunology--IM; Adult; Aged; Aged, 80 and over; Gastric Mucosa--Pathology--PA; Gastritis--Pathology--PA; **Helicobacter** pylori--Pathogenicity--PY; Middle Age; Phenotype; Pyloric Antrum--Immunology--IM; Pyloric Antrum--Pathology--PA; Th1 Cells --Chemistry--CH; Th1 Cells--Immunology--IM

1/9/6
DIALOG(R)File 155:MEDLINE(R)

09533716 98298031
Chronic active hepatitis induced by Helicobacter **hepaticus in the A/JCr mouse is associated with a** Th1 **cell-mediated immune response.**
Whary MT; Morgan TJ; Dangler CA; Gaudes KJ; Taylor NS; Fox JG
Division of Comparative Medicine, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA. mwhary@mit.edu
Infection and immunity (UNITED STATES) Jul 1998, 66 (7) p3142-8, ISSN 0019-9567 Journal Code: GO7
Contract/Grant No.: RO1 CA 67529, CA, NCI; RO1 DK 52413, DK, NIDDK; RR 07036, RR, NCRR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9809
Subfile: INDEX MEDICUS
Helicobacter hepaticus infection in A/JCr mice results in chronic active hepatitis characterized by perivascular, periportal, and parenchymal infiltrates of mononuclear and polymorphonuclear cells. This study examined the development of hepatitis and the immune response of A/JCr mice to H. hepaticus infection. The humoral and cell-mediated T helper immune response was profiled by measuring the postinfection (p.i.) antibody response in serum, feces, and bile and by the production of cytokines and proliferative responses by splenic mononuclear cells to H. hepaticus antigens. Secretory immunoglobulin A (IgA) and systemic IgG2a antibody developed by 4 weeks p.i. and persisted through 12 months. Splenocytes from infected mice proliferated and produced more gamma interferon (IFN-gamma) than interleukin-4 (IL-4) or IL-5 when cultured with H. hepaticus outer membrane proteins. The predominantly IgG2a antibody response in serum and the in vitro production of IFN-gamma in excess of IL-4 or IL-5 are consistent with a Th1 immune response reported in humans and mice infected with **Helicobacter** pylori and **Helicobacter** felis, respectively. Mice infected with H. hepaticus developed progressively severe perivascular, periportal, and hepatic parenchymal lesions consisting of lymphohistiocytic and plasmacytic cellular infiltrates. In addition, transmural typhlitis was observed at 12 months p.i. The characterization of a cell-mediated Th1

immune response to H. hepaticus infection in the A/JCr mouse should prove valuable as a model for experimental regimens which manipulate the host response to **Helicobacter** .
Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
Descriptors: **Helicobacter** --Immunology--IM; *Hepatitis, Chronic --Immunology--IM; *Th1 Cells--Immunology--IM; Antibodies, Bacterial--Blood --BL; Bile--Microbiology--MI; Cytokines--Biosynthesis--BI; Feces --Microbiology--MI; Hepatitis, Chronic--Pathology--PA; IgG--Blood--BL; IgG --Classification--CL; Lymphocyte Transformation; Mice
CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Cytokines); 0 (IgG)

1/9/7
DIALOG(R)File 155:MEDLINE(R)

09392512 98123801
Analysis of TH1 **and TH2 cytokine production in low grade B cell gastric MALT-type lymphomas stimulated in vitro with** Helicobacter **pylori.**
Hauer AC; Finn TM; MacDonald TT; Spencer J; Isaacson PG
Department of Paediatric Gastroenterology, St Bartholomew's School of Medicine, St Bartholomew's Hospital, London, UK.
Journal of clinical pathology (ENGLAND) Nov 1997, 50 (11) p957-9, ISSN 0021-9746 Journal Code: HT3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9804
Subfile: AIM; INDEX MEDICUS
Previous studies have suggested that the dependence of low grade B cell gastric lymphoma on infection of the gastric mucosa with **Helicobacter** pylori results from help provided by H pylori specific tumour infiltrating T cells. ELISPOT analysis was used to characterise functional subpopulations of tumour infiltrating T cells. The production of the TH1 cytokine interferon gamma and TH2 cytokines interleukin (IL)-4, IL-5, and IL-10 were measured in tumour cell suspensions from two cases of low grade B cell gastric lymphoma, one case of thyroid gland lymphoma, and one case of salivary gland lymphoma. Cells were assayed on day 0 and following 24 hours incubation either in culture medium or with a range of strains of H pylori. There was a dominant TH1-type (pro-inflammatory) response consistent with the TH1 response observed in H pylori gastritis.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: Antigens, Bacterial--Immunology--IM; *Cytokines --Biosynthesis--BI; * **Helicobacter** pylori--Immunology--IM; *Lymphoma, Mucosa-Associated Lymphoid Tissue--Immunology--IM; *Neoplasm Proteins --Biosynthesis--BI; *Stomach Neoplasms--Immunology--IM; Interferon Type II --Biosynthesis--BI; Interleukins--Biosynthesis--BI; Th1 Cells--Immunology --IM; Th2 Cells--Immunology--IM; Tumor Cells, Cultured
CAS Registry No.: 0 (Antigens, Bacterial); 0 (Cytokines); 0 (Interleukins); 0 (Neoplasm Proteins); 82115-62-6 (Interferon Type II)

1/9/8
DIALOG(R)File 155:MEDLINE(R)

09347315 98056706
Murine CD4 T-cell response to Helicobacter **infection: TH1 cells enhance gastritis and TH2 cells reduce bacterial load.**
Mohammadi M; Nedrud J; Redline R; Lycke N; Czinn SJ
Institute of Pathology, Case Western Reserve University, Cleveland, Ohio, USA.
Gastroenterology (UNITED STATES) Dec 1997, 113 (6) p1848-57, ISSN 0016-5085 Journal Code: FH3
Contract/Grant No.: DK-46461, DK, NIDDK; AI 40701-01, AI, NIAID; AI-36359 , AI, NIAID
Languages: ENGLISH

Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9803
Subfile: AIM; INDEX MEDICUS

BACKGROUND & AIMS: Previous findings suggest that TH1 cellular immune responses contribute to **Helicobacter** -associated gastritis. To further investigate this issue, interleukin 4 gene targeted mice were infected with **Helicobacter** felis, and a series of adoptive transfer experiments was performed to evaluate the role of both TH1 and TH2 cells. METHODS: Antigen-specific spleen cells from immunized/challenged or nonimmunized/infected mice or CD4+ T-cell lines were transferred adoptively into naive recipients before live bacterial challenge. RESULTS: Transfer of cells from both groups of donors as well as TH1 or TH2 cell lines exacerbated gastric inflammation in the recipients. No effect on bacterial load was observed in recipients of bulk spleen cells from infected mice or recipients of TH1 cell lines. In contrast, when either a TH2 cell line or bulk cells from immunized challenged mice were transferred adoptively, recipients showed a dramatic reduction in bacterial load. Increased numbers of bacteria were also noted in interleukin 4-deficient mice. CONCLUSIONS: These data suggest a differential contribution of TH1 and TH2 cell-mediated immune responses in **Helicobacter** infection: one associated with the pathogenesis of disease (TH1 phenotype) and the other associated with protection from or control of infection (TH2 phenotype).

Tags: Animal; Female; Support, U.S. Gov't, P.H.S.

Descriptors: CD4-Positive T-Lymphocytes--Physiology--PH; *Gastritis --Microbiology--MI; ***Helicobacter** ; ***Helicobacter Infections** --Immunology --IM; Adoptive Transfer; Antibodies--Analysis--AN; Cell Division --Physiology--PH; Cell Line; Colony Count, Microbial; Gastritis--Immunology --IM; Gene Targeting; **Helicobacter** --Isolation and Purification--IP; **Helicobacter** Infections--Microbiology--MI; Interferon Type II --Biosynthesis--BI; Interleukin-4--Genetics--GE; Mice; Mice, Inbred C57BL; Mice, Knockout; Th1 Cells--Physiology--PH; Th2 Cells--Physiology--PH

CAS Registry No.: 0 (Antibodies); 0 (Interleukin-4); 82115-62-6 (Interferon Type II)

1/9/9

DIALOG(R)File 155:MEDLINE(R)

08654676 96238941

Helicobacter **-specific cell-mediated immune responses display a predominant** Th1 **phenotype and promote a delayed-type hypersensitivity response in the stomachs of mice.**

Mohammadi M; Czinn S; Redline R; Nedrud J

Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106, USA.

Journal of immunology (UNITED STATES) Jun 15 1996, 156 (12) p4729-38, ISSN 0022-1767 Journal Code: IFB

Contract/Grant No.: DK 46461, DK, NIDDK; HL 37117, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9609

Subfile: AIM; INDEX MEDICUS

Studies regarding the nature of cell-mediated immunity in **Helicobacter** pylori infection and its role in pathogenesis have yielded controversial results. To address this issue in a controlled manner, we have employed the well-characterized **Helicobacter** felis-mouse model. Immunized/challenged and nonimmunized/infected mice were evaluated for cellular proliferation, gastric inflammation, and cytokine and Ab production at various times after infection. We observed two types of cell-mediated immune responses depending on the nature of the Ag preparation. The first response is a **Helicobacter** -independent response, present in all experimental groups, which is directed toward Ags such as urease and heat shock proteins. The second is a **Helicobacter** -dependent cellular response restricted to mice previously exposed to **Helicobacter** Ags either by immunization or infection. This response was not seen in noninfected controls. The

Helicobacter -dependent cellular response had a Th1 phenotype, as either infected or immunized/challenged mice demonstrated local and systemic production of IFN-gamma and undetectable levels of IL-4 or IL-5. Cellular proliferation correlated with the severity of gastric inflammation in both immunized/challenged (protected) and nonimmunized/infected mice. Finally, in vivo neutralization of IFN-gamma resulted in a significant reduction of gastric inflammation in H. felis-infected, as well as immunized/challenged, mice. This treatment also revealed the presence of Th2 cells, restricted to immunized/challenged mice, as demonstrated by local and systemic production of IL-4 in these mice. These data demonstrate that **Helicobacter** infection and/or immunization stimulate a predominantly Th1-type, Ag-specific response and promote a local delayed-type hypersensitivity response in the stomach that may be inhibited by depletion of IFN-gamma.

Tags: Animal; Female; Support, U.S. Gov't, P.H.S.

Descriptors: **Helicobacter** --Immunology--IM; *Hypersensitivity, Delayed --Immunology--IM; *Lymphocyte Transformation; *Stomach--Immunology--IM; *Th1 Cells--Immunology--IM; Gastritis--Immunology--IM; Immunity, Cellular; Interferon Type II--Physiology--PH; Mice; Mice, Inbred C57BL; Urease --Immunology--IM

CAS Registry No.: 82115-62-6 (Interferon Type II)

Enzyme No.: EC 3.5.1.5 (Urease)